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EDITORIAL COMMENT

Rethinking the Morbidity of Peripheral Arterial Disease and the "Normal" Ankle-Brachial Index*

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Peripheral arterial disease (PAD) is a common condition, estimated to affect 15% of the U.S. population above the age of 70 years (1). The ankle-brachial index (ABI) is a simple, noninvasive test that is used both to screen for PAD and to establish its diagnosis with a high degree of accuracy. In healthy adults without arterial occlusive disease, ankle systolic pressure is typically 10 to 15 mm Hg greater than arm (brachial) systolic pressure, due to the effect of pulse wave reflection. A truly normal ABI is above 1.10, although PAD is generally defined as a resting ABI of 0.90 or less (2,3).

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For decades, the ABI has been used as a basic tool of vascular practice to quantify the severity of occlusive disease among patients with leg symptoms and to decide if revascularization is needed. More recently, the ABI has diverged from this clinical use to become a marker of cardiovascular risk. In multiple studies and a recent meta-analysis of >47,000 subjects, the presence of an abnormal ABI has been shown to increase the risk of myocardial infarction and death, among other adverse outcomes, and to improve upon the prognostic capabilities of the Framingham risk score (4–6). Given these data, professional societies have called for the use of the ABI as a tool for cardiovascular risk stratification and the identification of patients who require more aggressive risk factor modification (2,3). Indeed, it seems that there has been a more recent focus on the link between PAD and heart disease in the medical literature than on the morbidity of PAD itself.

With this proliferation of high-quality epidemiologic research on PAD as a coronary risk equivalent, it is possible to overlook that PAD is a potentially disabling disease of the legs. In this issue of the *Journal*, McDermott et al. (7) remind us of the very practical origins of the ABI as a test to evaluate leg pain. The authors extend their groundbreaking work on functional decline and PAD to investigate the association of borderline and low normal ABI values with progressive functional impairment (7).

In the WALCS (Walking and Leg Circulation Study), patients with and without PAD were identified from vascular laboratories and ambulatory care practice and were followed up for 5 years with annual ABI measurement, functional assessment, and a questionnaire for mobility loss. Mobility impairment was defined as the self-reported loss of the ability to walk one-quarter of a mile or navigate a single flight of stairs without help or the inability to complete a 6-min walk test. Patients were categorized according to the lower ABI of the 2 limbs at baseline, including normal ABI (1.10 to 1.30), PAD (ABI <0.90), as well as borderline PAD (ABI 0.90 to 0.99) and low normal ABI (ABI 1.00 to 1.09). Consistent with prior studies, subjects with ABI <0.90 were more likely to develop mobility impairment during the follow-up period than were subjects with normal ABI, with the greatest risk among subjects with ABI <0.50 at baseline (hazard ratio: 4.16) (8,9). Notably, subjects with low normal ABI and borderline PAD also had a significant risk of mobility loss during follow-up (hazard ratios: 2.61 and 3.07, respectively). The likely mechanism of functional decline among subjects with ABI 0.90 to 1.09 was progressive arterial occlusive disease. During the 5 years of follow-up, 50% of subjects with borderline PAD (ABI 0.90 to 0.99) and 17% of patients with low normal (1.00 to 1.09) had a decline in ABI value to <0.90, and the association between mobility loss and borderline and low normal ABI was attenuated after adjustment for disease progression. Quality of life data from this cohort would be of interest, although they are not reported here. Nonetheless, these are important new data establishing the potential for progressive functional impairment and disability among patients previously classified as "normal" in the noninvasive vascular laboratory.

This study serves as a reminder of the morbidity associated with PAD. While the classic symptom of intermittent claudication is reported in less than one-quarter of patients with PAD (8,10), even those with atypical leg symptoms or no self-reported leg symptoms have impaired walking abilities (8). Peripheral arterial disease impairs quality of life and has even been associated with symptoms of depression (11–13).

What therapies are available to patients with leg symptoms and/or functional impairment due to PAD? Although supervised exercise rehabilitation is the single most effective treatment for claudication, it is not available to most patients because of absent reimbursement for such programs by third-party payers (14). Home-based and partially super-

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vised exercise training programs require further development and study. It has been more than a decade since the Food and Drug Administration has approved a new drug for the treatment of claudication (namely, cilostazol in 1999), and there are only 2 drugs available to patients. Despite the dramatic upsurge in the performance of catheter-based revascularization procedures to treat leg symptoms related to PAD, the effectiveness and sustained benefit of this strategy are unproven. Aside from supervised exercise, there are no proven therapies to prevent or reverse functional decline and mobility loss among patients who have atypical leg symptoms, the majority of the PAD population (15). The identification of effective therapies to improve function and quality of life and to prevent disability among patients with PAD, across the entire spectrum of disease, is an area of great unmet medical need.

Finally, McDermott et al. (7) draw attention to the evolving concept of the "normal" ABI. Although an ABI cut-point of 0.90 is used in most vascular laboratories for the diagnosis of PAD and is the diagnostic criterion of the 2 major PAD practice guidelines, an ABI of <1.10 is not normal (2,3). A patient with low normal or borderline ABI at rest should undergo repeat ABI measurement after treadmill (or other) exercise, a procedure that will result in a significant fall in ABI in up to one-half of patients (16,17). If exercise is not possible, these patients should be identified as having subclinical PAD and followed up for disease progression.

Low normal and borderline ABI values increase cardiovascular risk and the likelihood of subclinical atherosclerosis in other vascular beds (4,5,18), and a normal ABI at rest that falls with exercise predicts adverse outcome (17). Now it has been established that an ABI of <1.10 is associated with progressive functional decline and mobility loss (7). The ABI is a stalwart tool, but there is a need for updated consensus guidelines as to its optimal interpretation in vascular practice.

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REFERENCES

1. Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999–2000. Circulation 2004;110:738–43.
2. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary: a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease). J Am Coll Cardiol 2006;47:1239–312.
3. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg 2007;45 Suppl S:5–67.
4. Fowkes FG, Murray GD, Butcher I, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. JAMA 2008;300:197–208.
5. Lee AJ, Price JF, Russell MJ, Smith FB, van Wijk MC, Fowkes FG. Improved prediction of fatal myocardial infarction using the ankle brachial index in addition to conventional risk factors: the Edinburgh Artery Study. Circulation 2004;110:3075–80.
6. Criqui MH, Langer RD, Fronek A, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. N Engl J Med 1992;326:381–6.
7. McDermott MM, Guralnik JM, Tian L, et al. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: the WALCS (Walking and Leg Circulation Study). J Am Coll Cardiol 2009;53:1056–62.
8. McDermott MM, Liu K, Greenland P, et al. Functional decline in peripheral arterial disease: associations with the ankle brachial index and leg symptoms. JAMA 2004;292:453–61.
9. McDermott MM, Ferrucci L, Simonsick EM, et al. The ankle brachial index and change in lower extremity functioning over time: the Women's Health and Aging Study. J Am Geriatr Soc 2002;50:238–46.
10. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA 2001;286:1317–24.
11. Schneider JR, McHorney CA, Malenka DJ, McDaniel MD, Walsh DB, Cronenwett JL. Functional health and well-being in patients with severe atherosclerotic peripheral vascular occlusive disease. Ann Vasc Surg 1993;7:419–28.
12. Regensteiner JG, Hiatt WR, Coll JR, et al. The impact of peripheral arterial disease on health-related quality of life in the Peripheral Arterial Disease Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program. Vasc Med 2008;13:15–24.
13. Arseven A, Guralnik JM, O'Brien E, Liu K, McDermott MM. Peripheral arterial disease and depressed mood in older men and women. Vasc Med 2001;6:229–34.
14. Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. JAMA 1995;274:975–80.
15. McDermott MM, Ades P, Guralnik JM, et al. Treadmill exercise and resistance training in patients with peripheral arterial disease with and without intermittent claudication: a randomized controlled trial. JAMA 2009;301:165–74.
16. Stein R, Hriljac I, Halperin JL, Gustavson SM, Teodorescu V, Olin JW. Limitation of the resting ankle-brachial index in symptomatic patients with peripheral arterial disease. Vasc Med 2006;11:29–33.
17. Feringa HH, Bax JJ, van Waning VH, et al. The long-term prognostic value of the resting and postexercise ankle-brachial index. Arch Intern Med 2006;166:529–35.
18. McDermott MM, Liu K, Criqui MH, et al. Ankle-brachial index and subclinical cardiac and carotid disease: the multi-ethnic study of atherosclerosis. Am J Epidemiol 2005;162:33–41.

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